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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,987	10/07/2003	Bruce A. Malcolm	JB01587	4551

24265 7590 07/11/2006

SCHERING-PLOUGH CORPORATION  
PATENT DEPARTMENT (K-6-1, 1990)  
2000 GALLOPING HILL ROAD  
KENILWORTH, NJ 07033-0530

EXAMINER
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STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/679,987	MALCOLM ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Teresa E. Strzelecka	1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 May 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 4-6 and 15-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 7-14 and 18-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>1/22/04; 2/11/04</u> .  | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of species of RNA-dependent RNA polymerase from Hepatitis C virus (claims 2, 3, 13 and 14) and hybridizing ppynucleotide comprising poly(G) and poly (C) (claims 7 and 18) in the reply filed on May 1, 2006 is acknowledged.
2. Claims 4-6 and 15-17 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 1, 2006.

### *Information Disclosure Statement*

3. The information disclosure statements (IDSs) submitted on January 22, 2004 and February 11, 2004 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

### *Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 9-12 and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Karamohamed et al. (Biotechniques, vol. 24, pp. 302-306, 1999).

Claims 1 and 12 will be considered together in claim 12, which is a species of claim 1.

Regarding claims 1 and 12, Karamohamed et al. teach a method of detecting RNA polymerase activity, the method comprising:

(a) providing a primer oligonucleotide having a 3' OH (page 302, last paragraph; page 303,

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first paragraph; page 304, second paragraph);

(b) contacting said primer oligonucleotide with a template polynucleotide and allowing hybridization to occur to form a hybridized polynucleotide (page 302, last paragraph; page 303, first and second paragraph; page 304, second paragraph);

(c) adding an RNA-dependent polymerase to said hybridized polynucleotide to produce a mixture (page 303, first and second paragraph; page 304, second paragraph);

(d) adding a PPI detection mixture to said mixture (page 303, second paragraph; page 304, second paragraph);

(e) adding a substrate mixture comprising a nucleotide triphosphate or an analog thereof to said mixture (page 303, second paragraph);

(f) adding a compound that is or is suspected of being an inhibitor of said RNA-dependent polymerase (page 303, third paragraph; page 304, fifth paragraph; Table 2); and

(g) measuring a product of the PPI detection mixture (page 303, last paragraph; page 304, first and second paragraphs, Fig. 1-3);

wherein apyrase is not part of the mixture (Table 1; page 303, second paragraph), and steps (c), (d), (e) and (f) may be performed simultaneously or separately in any order.

Regarding claims 9 and 20, Karamohamed et al. teach detection mixture comprising luciferase, luciferin, ATP sulphurylase and AP, with the product being emitted light (page 303, second paragraph; Table 1).

Regarding claims 10 and 21, Karamohamed et al. teach measuring light with a luminometer (page 303, second paragraph).

Regarding claims 11 and 22, Karamohamed et al. teach a luciferase operating at 23° C (page 303, last paragraph). Since Applicants did not define the term “thermostable”, the luciferase of

Karamohamed et al. is inherently thermostable up to 30° C (page 304, fourth paragraph). Further, Karamohamed et al. teach luciferase stable at higher temperatures (page 306, first paragraph).

*Claim Rejections - 35 USC § 103*

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 2, 3, 7, 8, 13, 14, 18 and 19 rejected under 35 U.S.C. 103(a) as being unpatentable over Karamohamed et al. (Biotechniques, vol. 24, pp. 302-306, 1999) and Lohmann et al. (J. Viral Hepatitis, vol. 7, pp. 167-174, 2000; cited in the IDS).

A) The teachings of Karamohamed et al. are presented above. They teach detection of reverse transcriptase activity, but do not teach RNA-dependent RNA polymerase from Hepatitis C virus or specific primers and templates.

B) Regarding claims 1-3 and 12-14, Lohmann et al. teach evaluation of Hepatitis C virus NS5B activity in the presence and absence of inhibitors (Abstract; page 169, last paragraph; Fig. 2; page 170, first and last paragraphs; page 171, paragraphs 1-3; Fig. 3).

Regarding claims 7 and 18, Lohmann et al. teach synthetic poly(G) and poly (C) (page 171, last paragraph).

Regarding claims 8 and 19, Lohmann et al. teach the primer and template polynucleotide being the same molecule (page 169, last paragraph; Fig. 2).

It would have been prima facie obvious to one of ordinary skill in the art to have tested the RNA polymerase of Lohmann et al. using the method of Karamohamed et al. The motivation to do

so, provided by Lohmann et al., would have been, as stated by Lohmann et al. (page 167, first two paragraphs):

“The hepatitis C virus (HCV) is a major causative agent of sporadic and transfusion-associated liver disease worldwide [reviewed in 1,2]. The majority (80±90%) of all infections become persistent and lead to various clinical outcomes ranging from an inapparent carrier state with almost normal liver function to chronic active hepatitis. Overall, ~ 50% of all infections lead to chronic hepatitis with 20% of those developing liver cirrhosis. Furthermore, patients with chronic hepatitis C, in particular those with cirrhosis, are at high risk of developing hepatocellular carcinoma, and HCV is the second most common aetiologic agent in the development of this disease. Chronic hepatitis C, to date, can only be treated with interferon-a (IFN-a). However, non-responders and relapsers are frequent, and sustained biochemical response is achieved in only ~20% of patients [reviewed in 3]. Although this number can be increased by combination therapy with the nucleoside analogue ribavirin, recent data indicate that even in this case at best 40% of treated patients show a sustained response and the number falls to 16% in IFN-a nonresponders [3]. Therefore, a more effective antiviral therapy is urgently required.”

The motivation to do so, provided by Karamohamed et al., would have been as stated by Karamohamed et al. (page 306, last paragraph):

“In conclusion, we present a real-time assay for continuous detection of RT activity. The assay is simple, sensitive and non-electrophoretic, and there is no need for labeled nucleotides. The applications of the assay are very broad, which opens up new possibilities for obtaining a detailed picture of the events involved in RT reactions, such as the effects of different compounds on RT activity.”

8. No claims are allowed.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka  
Primary Examiner  
Art Unit 1637

*Teresa Strzelecka*  
7/18/06